**GI DRUGS MOST IMPORTANT DRUG NAMES TO REMEMBER**

* **CIMETIDINE**
  + H2 blocker, blocks met of drugs by P450 oxidases; antiandrogenic (galactorrhea in F, impotence & gynecomastia in men)
* **OMEPRAZOLE**
  + irreversible PPI, delivered to stomach via the blood, has either enteric coating or w/NaHCO3 to avoid activation in the stomach, oral or injected & used short & long term. Worries: cancer of ECL cells? & higher pH allowing bacterial growth, hypoMg, fractures. Inhibits CYP2C19 & 3A4 so blocks Diazepam & Clopidogrel. Drug interactions due to higher pH🡪 less keoconaole, Fe salts, ampicillin, atazanavir & more Digoxin
* **MISOPROSTOL**
  + Prostaglandin E2 derivative. Increases blood flow, mucous and decreased acid. SE= diarrhea & uterine contraction. Contraindicated in pregnancy!
* **SUCRALFATE**
  + polymerizes pH<4 so coats for 6 hours.Interacts w/absorption of drugs: Cimetidine, Omeprazole, Tetracyclines & antacids contraindicated for 30 min after
* **BISMUTH SUBSALICYLATE** 
  + precipitates if pH<4 so coats ulcer & kills H.pylori
* **MAGNESIUM AND ALUMINUM HYDROXIDE**
  + Antacids; Mg increases motility (diarrhea) & Al decreases motility (constipation) so they’re often mixed.Ca,Mg,Al inhibit absorption of tetracyclines & quinolones. Causes gastric pH to rise. And watch for cation toxicity if renal fxn is impaired.
* **TETRACYCLINE, METRONIDAZOLE**
  + antibiotics. H pylori becomes R to metrodinazole & clarithromycin so use more 2 or more
* **MAGNESIUM HYDROXIDE** 
  + Antacid reacts quickly at pH 8-9
* **MgSO4** 
  + osmotic fast acting laxative. Works in 1-3 hrs. Can cause Mg toxicity if renal fxn impaired. Can be used for drug overdose.
* **SORBITOL** 
  + Osmotic fast acting laxative. Can be used for drug overdose
* **PSYLLIUM**
  + A Fiber; binds water to reduce watery stool & create distention to improve gastric motility; binds Digoxin & warfarin. Lowers cholesterol by binding bile acids.
* **PHENOLPHTHALEIN**
  + Stimulant laxative works in colon due to enterohepatic cycling of glucuronides. Effects seen 6-8 hours. Withdrawn from market due to tumors in rats. Can cause hypoK.
* **BISACODYL**
  + Stimulant laxative works in the colon due to enterohepatic cycling of glucoronides and acts within 6-8 hours. Can’t chew or crush or will vomit. Can cause hypokalemia. Chronic use NOT recommended. Secreted in saliva, breast milk, urine.
* **SENNA**
  + Stimulant laxative that contains danthron glycosides and act in the colon. Secreted in saliva/breast milk/urine.
* **DOCUSATE**
  + Stool softener (lubricant, emulsifier, detergent). Mild laxation produced in 1-3 days.
* **CASTOR OIL**
  + Ricinoleic acid causes peristalsis/secretion of SI & colon. Complete emptying! NOT recommended for common constipation! Induce uterine contraction in pregnant women.
* **CISAPRIDE** 
  + 5-HT4 Receptor agonist used for GERD, diabetic gastroparesis, chronic constipation. Causes arrhythmias bc oxidized by CYP3A4 so don’t take with CYP inhibitor.
* **METOCLOPRAMIDE**
  + agonist at 5-HT4 receptors & antagonist at D2 & 5-HT3 receptors. Used for GI motility for gastroparesis, GERD and as anti-nausea to prevent N/V associated with chemotherapy. Serious side effect = Tardive dyskinesia.
* **DICYCLOMINE** 
  + Antimuscarinic used for IBS. Decreases motility. Don’t use if patient has GERD, UC, or glaucoma.
* **DIPHENOXYLATE AND LOPERAMIDE**
  + Opiod agonists that inhibit Ach release in the myenteric plexues. Decreases motility but increases GI muscle tone especially sphincters. Diphenoxylate- At typical doses no analgesia or euphoria. Higher doses can be so mixed. with atropine to limit abuse potential. Loperamide- Pumped out of the CNS so no analgesia/euphoria. Contraindicated for UC b/c may precipitate toxic megacolon.
* **PROCHLORPERAZINE**
  + ANTIemetic. Antagonist at D2,M, H1, 5-HT receptors. Reserved for when N/V is resistant to other drugs. Side effects due to dopamine antagonism (parkinsonism.)
* **SYRUP OF IPECAC**
  + Induces vomiting after drug overdose by acting in intestines & CTZ. Toxic doses damage liver, kidney, heart, & skeletal muscle. Chronic abuse cause CHF/myopathy.
* **ONDANSETRON**
  + Antagonist at 5-HT3 receptors. Effective in treating acute vomiting.
* **SCOPOLAMINE**
  + Antimuscarinic used for prophylaxis of motion sickness (most efficacious).
* **DIPHENHYDRAMINE AND DIMENHYDRINATE**
  + Antimuscarinic & antihistamine effects contribute to prevention of motion sickness. Sedative and anti-muscarinic effects.
* **PROMETHAZINE**
  + M & H1 antagonist. Prevents N/V in surgery. Prevents motion sickness. Has sedative & antimuscarinic side effects. Can cause respiratory depression so contraindicated in kids under 2. Can cause potential limb loss if into the artery.
* **MECLIZINE**
  + Antihistamine that produces less sedation and used for milder cases of motion sickness.
* **SULFASALAZINE**
  + Treatment of UC, CD, and RA. Prodrug cleaved by bacteria in the gut to become active 5-ASA which inhibits COX-2 and 5-lipoxygenase.
* **BALSALAZIDE**,
  + Newer prodrug taken orally that releases 5-ASA and cleaved by bacteria. Better than sulfasalazine for CD and used for mild-moderate UC. Better tolerated, fewer side effects.
* **MESALAMINE OR 5-AMINOSALICYLATE (5-ASA)** 
  + Active ingredient in sulfalazine & balsalazine; Indication UC. Oral or rectal use suppositories. Inhibits COX-2 and 5-lipoxygenase
* **CROMOLYN SODIUM**
  + prevents activation of mast cells. Treats UC and systemic mastocytosis.
* **INFLIXIMAB** 
  + Chimeric human-mouse monoclonal Ab to TNFa. Used with methotrexate. Treats moderate-severe Crohn’s and UC that’s unresponsive. Expensive!
* **PREDNISONE**- systemic GC; treating acute CD exacerbations. Don’t use for maintenance due to SE.
* **PREDNISOLONE**- systemic GC; treating acute CD exacerbations. Don’t use for maintenance due to SE.
* **BUDESONIDE**-
  + GC with high topical activity for mild-moderate CD. Also treats asthma. High first pass metabolism. Enteric coated and delayed release formulation to retain in gut until distal ileum and ascending colon. Much variability in “delay” of action.

**DIABETES DRUGS MOST IMPORTANT DRUG NAMES TO REMEMBER**

* **INSULIN LISPRO**
  + Ultra short acting insulin
  + B/c the amino acid sequence on the B-chain of this insulin has 2 AA switched it inhibits formation of hexameras w/ Zn so no dissociation necessary
  + OOA—5-15 min; PPC—30-90 min; DOA—3-4 hr
    - Should be administered 0-15 min before a meal (less time than regular insulin)
    - Disappears faster so ↓ risk of hypoglycemia
  + Soluble so can be give IV---solution has a pH <4
* **REGULAR INSULIN (HUMULIN)**
  + Short acting insulin
  + Zn2+ insulin solution
  + Released moderately quickly from SC sites
  + OOA—30 min PPC—1-2 hr DOA 5-8 hr
    - Administer 30-60 min before eating!
  + ONLY TYPE THAT CAN BE ADMINISTERED IV/IM in an emergency situation (diabetic coma)—must be in solution when you inject it
* **NPH INSULIN/ISOPHANE INSULIN** 
  + Intermediate acting insulin—administered SC
  + Suspension of crystal zinc insulin combined with 1 protamine (+) charge—so this is not in solution
  + MAY BE MIXED WITH REGULAR INSULIN—b/c it wont effect the absorption of the regular insulin
  + No useful in emergency situations
  + Slow absorption b/c it is a suspension so
    - OOA—2-4 hr; PPC—6-12 hr; DOA—16-24 hrs
* **INSULIN** **GLARGINE**
  + Long acting insulin
  + Modified human insulin—its not soluble unless the pH is <4; forms microppt at pH 7 after SC injection
  + Contains Zn2+
  + Zero order absorption
    - Administered once daily at bedtime—to provide low levels of insulin during period of long fasting (sleep)
  + OOA—2-3 hr; PPC—no peak but plateaus; DOA—24+ hrs
  + DO NOT MIX WITH OTHER INSULINS—lispro solution is at a pH <4
* **TOLBUTAMIDE**
  + 1st generation Sulfonylureas (K+ channel blocker)
  + Blocks the K channel which causes depolarization of the PM which causes Ca channel to open and insulin gets released—DON'T NEED GLUCOSE TO FOR THIS DRUG TO STIMUALTE INSULIN (risk for hypoglycemia)
  + \*\*remember drugs that open K channels (Diazoxide, minoxidil, and HCTZ) all can lead to hyperglycemia b/c ↓ release of insulin
  + shortest t1/2 life of these—5 hrs; SAFEST in elderly patients
* **GLYBURIDE**
  + 2nd generation Sulfonylureas (K+ channel blocker)
  + t ½ is 10 hrs
  + more potent
* **REPAGLINIDE**
  + Is a meglitinide
  + Binds to the sulfonylurea receptor (at a different site than the sulfonylureas) and blocks the K channel🡪 stimulates release of insulin
  + Rapid OOA and short DOA (t1/2 1hr)
  + Administered 3-4x’s per day before each meal—mimics physiological insulin profile
* \*\*\*\*Tolbutamide, Glyburide and Repaglinide—all exhibit tachyphylaxis
  + Resistance to these drugs can develop maybe b/c as the disease progresses ↓ # of β cells (↓ insulin), ↓ muscle mass (↓ glucose uptake ability), ↓ physical activity (↓ glucose transporters in skeletal muscle)
* **GLUCAGON**
  + Can be used to treat severe hypoglycemia
  + Administer SC, IV, IM—follow it with carbs
  + Effects are not blocked by β blockers (EPI effects are)
  + Limitation—glucose stores must be available so not useful in starved patients. Less effective in type 1 than type 2 DM
* **METFORMIN**
  + It is a biguanide
  + Promotes action of insulin (especially in the liver—INHIBITS HEPATIC GLUCONEOGENESIS) and ↑ peripheral glucose uptake
  + DOES NOT induce insulin release (ONLY USED IN TYPE 2/INSULIN RESISTANT DM)
  + Administer w/ meals b/c need insulin and glucose to work
  + ↓ fasting hyperglycemia, ↓ post-prandial hyperglycemia, and rarely induces hypoglycemia
  + can be combined w/ sulfonylureas, acarbose, glitazones
  + KIDNEY ELIMINATION (very water soluble)—DM and elderly are most common ppl to have ↓ renal function so in patients w/ impaired kidney function this drug can accumulate and ↑ side effects which are transient N/V/D, weight loss ☺, impair vit B12 and folate absorption (rarely leads to pernicious anemia), LACTIC ACIDOSIS (so monitor renal function while on this drug can it can lead to this if its not cleared)
  + Drug interactions—cationic drugs, IV iodinated contrast materials like those used in urogrames, cholangiography, angiography, CT b/c they impair kidney function
  + Surgical procedures ↓ renal function so suspend metformin therapy and resume when the patients renal function is back to normal
  + Contraindications—CHF or MI (hypoxic states—b/c these states promote lactic acidosis), Liver disease (important for lactate metabolism), excessive alcoholism (potentiates effect on metformin on lactate metabolism)
* **ROSIGLITAZONE**
  + It is a thiazolidinediones
  + Used for type 2 DM
  + AGONIST FOR PPAR γ –regulates synthesis of insulin-responsive genes (↓ lipolysis, ↑ glu uptake, ↑ glu utilization)
  + REQUIRES INSULIN and PROMOTES INSULIN ACTIONS IN ADIPOSE TISSUE AND MUSCLE—works at diff sites than metformin so you can combine the two
  + LIPID SOLUBLE SO EXTENSIVE METABOLISM BY THE LIVER –monitor liver enzymes b/c may become toxic to the liver
  + Takes hours to see effects—administered 1-2x’s per day INDEPENDENT OF MEALS
  + ↓ fasting hyperglycemia, ↓ post-prandial hyperglycemia, and rarely induces hypoglycemia
  + Side effects—WEIGHT GAIN ☹--if used with metformin can counteract this some but not all the way, also causes edema, liver toxicity, risk of fractures in women, HEART FAILURE
  + Adverse effects of just rosiglitazone—CARDIAC ISCHEMIA, ANGINA, MI
  + Label now says that patients that are already on this can stay on this but it shouldn't be newly prescribed unless blood glucose can be controlled and patient doesn't want to be on piolglitazone (b/c ↑ risk of bladder CA)
* **ACARBOSE**
  + α glucosidase inhibitor
  + TYPE 2 DM
  + Competitive inhibition of α-disaccharidases in proximal small intestine
    - Slows down abs of most carbs
  + ↓ post-prandial hyperglycemia by 45-60
  + NO HYPOGLYCEMIA when used alone but can be used w/ sulfonylureas
  + ADMINISTED AT THE START OF A MEAL
  + Side effects—flatuelence, diarrhea, small weight loss
  + Contraindication—IBD
  + Metabolized in the GI tract and eliminated in feces
* **PRAMLINTIDE**
  + Analog of amylin (amylin is also released from β cells along with insulin)
  + Good for patients w/ type II DM
  + Inhibits post-prandial glucagon secretion
  + slow down gastric emptying, ↓ rise in blood glucose, inhibits glucagon release, ↓ appetite by working in CNS
  + NET: glucose enters blood more slowly
  + Used to improve glycemic control in patient who have failed to achieve desired glucose control
  + SC injection prior to major meal with short acting insulin (BUT DO NOT MIX b/c pH of this is acidic)
  + Effects: ↓ plasma glucose fluctuations (can produce severe hypoglycemia so don't use if you have “hypoglycemia unawareness”), ↓ HbA1C, ↓ weight, **↓ required dose of insulin**
* **EXENTAIDE**
  + GLP-1 like peptide (found in venom of Gila monster)
  + Stimulates insulin and amylin release but need glucose for it to work b/c need the ATP to close the K channel and depolarize the cell and open Ca channels
  + TYPE 2 DM ONLY
  + ↓ postprandial and fasting plasma glucose
  + Inhibits glucagon, slows stomach emptying, ↓ appetite via CNS
  + Side effects—N/V/D, ↑ hypoglycemia risk if used w/ sulfonylurea
  + Potential problems—ACUTE PANCREATITIS, ↓ RENAL FUNCTION
* **SITAGLIPTIN**
  + Inhibit dipeptidyl peptidase -4 (DDP-4)
    - Inhibits inactivation of incretins GLP-1 and GIP so increases GLP-1 and GIP in the blood 2-3 fold
  + Glucose-dependent stimulation of insulin
  + TYPE 2 DM
    - To improve glycemic control, monotherapy adjunct to diet and exercise, combo w/ metformin
  + ELMINATED BY KIDNEY (like metformin)—so dose is adjusted according to kidney function
  + POTENTIAL PROBS—ACUTE PANCREATITS

**ANDRENAL DRUGS**

* **PREDNISONE—**short acting GC; not active—must go to liver and get activated into prednisolone; has 4x’s antiinflamm activity of cortisol by only 0.3x’s its mineralcorticoid activity. No topical activity. Given orally
* **PREDNISOLONE** –Same actions as prednisone but can be used topical
* **TRIAMCINOLONE—**intermediate acting GC; Has 5x cortisol topical activity. No salt retaining ability. Can convert it into **ACETONIDE** and its topical activity goes up to 100x’s cortisols (beneficial in tx of asthma)
* **DEXAMETHASONE—**long acting GC; This drug is so potent so ↑ risk for side effects. Use these for cerebral edema (child w/ seat belt on gets in MVA w/ head trauma🡪 ↑ inflammation and swelling in the head so give this to tx the inflammation and not increase BP.
* **FLUDROCORTISONE—**mineralcorticoid; 250x’s aldosterones salt retaining ability.

**COMPLICATIONS AND WHAT TO TREAT WITH**

* **REPLACEMENT THERAPY** (adrenal insufficiency)
  + Hydrocortisone & Fludrocortisone
* **PALLITATIVE THERAPY**
  + ARTHRITIS AND TENDINITIS—Prednisolone
  + ALLERGY AND ASTHMA—Triamcinoone acetonide, Budesonide, Gluticason
  + DERMATOLOGICAL DISORDERS—topical ones
  + AUTOIMMUNITY—oral prednisone
  + ORGAN TRASPLANTATION—prdnisone & cyclosporine
  + MALIGNANCIES—prednisone
  + PREMATURE BIRTH--↑ surfactant w/ GC
  + GI DISORDERS
  + CEREBRAL EDEMA—Dexamethasone
  + HYPERCALCEMIC
  + SHOCK
  + COLLAGEN VASCULAR DISORDER
  + NEUROMUSCULAR DISORDERS
  + RENAL DISEASES
  + HEMATOLOGICAL DISORDERS

**ANTI-ADRENOCORTICOSTEROIDS**—useful in tx of disease of adrenal hyperactivity (Cushing, Conn)

* **INHIBITORS OF ADRENAL STEROID BIOSYNTHESIS**
  + **AMINOGLUTETHIMIDE**—inhibits conversion of cholesterion to 20-α-hydroxycholesterol; blocks production of all steroids from adrenal cortex
    - Used as adjunct in cushing, used to tx breast and prostate cancer (↓ estrogen)
  + **MEYRAPONE**—inhibits 11-β-hydroxylation of steroids
    - Blocks aldosterone and cortisol
    - Used as adjunct in cushing and to test pituitary ability to respond to ↓ levels of GC’s
* **ANTAGONIST**
  + **SPIRONOLACONE**—competitive antagonist to both mineralcorticoid and androgen recepotrs
    - Used as diuretic, to tx hirsutism, Conn’s
    - Cause hyponatremia/hyperkalemia, metabolic acidosis, gynecomastia, impotence
  + **EPLERENONE**—aldosterone antagonist
  + **RU486 (MIFEPRISTONE)—**anti progesterone and also potent anti-GC
    - Used in Cushing sx

**THYROID DRUGS**

**DRUGS FOR HYPOTHYROIDISM**

* **POWDERED THRYOID GLAND—**cheap, difficult to control, hypersensitivity rxns,
* **LEVOTHYROXINE SODIUM—**synthetic T4; Allergies can be developed to the filler, only once daily dosing. DOC
* **LIOTHYRONINE SODIUM—**pure T3; if patient presents w/ myxedema coma use this; THIS IS POTENT. CARDIOTOXIC
* **LIOTRIX—**4:1 T4:T3;

**DRUGS FOR HYPERTHYROIDISM**

* **THIONAMIDES—**Propylthiouracil (PTU), Methimazole, Carbimazole (10x’s more potent than PTU)
  + **INHIBITS THYROID PEROXIDASE**—block tyrosine iodination on TGB, block iodotyrosine coupling, PTU block deiodination of T4🡪T3
  + PTU needs multiple daily dosing; methimazole one need once a day. These do not block the release of thyroid hormone. Takes weeks to see ↓ in thyroid hormone.
  + Side effects: rashes, fever, vasculitis, arthralgia, cholestatic jaundice, hepatitis; hypothyroidism w/ prolonged or excessive tx
    - ↑ incidence of liver failure w/ PTU.
  + Advantage—avoids surgery and reversible; Disadv--↑ incidence of relapse and remission takes years.
  + Methimazole is first line drug for young patients w/ mild—moderate dz
  + PTU is second ling drug therapy unless the patients are allergic or intolerant to methimazole
  + Used as adjuncts to surgical removal or radioactive ablation of hyperthyroid gland to normalize the patient
* **IONIC INHIBITORS**
  + Thiocyanate (SCN-)—blocks the uptake of iodide
  + Perchlorate (ClO4)—blocks uptake of iodide—now is a dx agent for thyroid function
* **IODIDE—**inhibits TH synthesis and release—often used along w/ β blockers to tx thyroid storm. ↓ size and vascularity of thyroid gland. Rapid action. No used for long term.
* **RADIOACTIVE IODINE—**131—only isotope used to tx hyperthyroidism. 123 is used in clinical dx.
  + Effect—necrosis of follicle cells
  + Adv—only thyroid is effected, surfery avoided, inexpensive.
  + Disadvantage--↑ incidence of delayed hypothyroidism; potential carcinogen; crosses placenta SO FEMALE CANT BE PREGS. Can obliterate parathyroid gland b/c proximity to thyroid gland.